# Supplementary materials

## Methods

SELECT-AXIS 2 (NCT04169373) was conducted using a master protocol with a common screening platform to determine patient eligibility into two separate phase 3, randomized, double-blind, placebo-controlled multicentre studies: bDMARD-IR or nr-axSpA. These two studies had several overlapping eligibility criteria. The ability to use a common screening platform is considered one of the main advantages of incorporating these two studies into a single master protocol, resulting in a decreased patient burden during screening and more efficient recruitment of subjects and use of resources. A patient determined to have an IR to bDMARD(s) during screening may be eligible for and randomized into one of the two studies without the need to screen-fail and rescreen for the other study. Patients were required to meet the modified New York criteria using confirmation of radiographic evidence by a central reader to be eligible for the AS bDMARD-IR study; however, those patients who do not meet these radiographic criteria may still be eligible for the nr-axSpA study. Despite the common screening platform and shared design elements, each study has its own objectives, hypothesis testing, randomization, data collection, and adequate power for primary and secondary endpoints. There is no overlap in the patient population, nor is there a shared control group. The success of each study in its corresponding patient population will be determined separately and independently of the other study. Each study represents a standalone study for regulatory purposes with the ability to report interim and final data independently; the results of the individual studies are published separately.

Patients in remission at week 104 have the option to enrol in a remission-withdrawal period.

Two separate randomization schedules were generated for Japan and China.



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An ASAS40 response was defined as an improvement of ≥40% and an absolute improvement from baseline of ≥2 units on a scale of 0–10 in at least three of the four domains: patient's global assessment of disease activity, patient's assessment of total back pain, BASFI, and inflammation assessed by morning stiffness (mean score of BASDAI questions 5 and 6), without worsening in the remaining domain.[25]

MRI of the spine and sacroiliac joints was performed during the screening period prior to or at the baseline visit and week 14 visit. MRIs were independently assessed by two readers blinded to treatment allocation and imaging time points. Discrepancies between the readers were resolved through adjudication by a third reader if scoring differences exceeded a certain mean absolute difference threshold.[21] The adjudication trigger for MRI of the spine was >14 and for MRI of the sacroiliac joints was >8.

For binary efficacy endpoints, the CMH test was conducted on each of the 30 datasets generated by NRI-MI, and the results were integrated using Rubin's rule.[46] The number of responders for binary efficacy endpoints was based on the total number of patients and MI-aggregated response rates. For continuous endpoints, the MMRM included treatment group, visit, and treatment-by-visit interaction as fixed effects and the corresponding baseline value and the stratification factor of screening hsCRP as covariates. The ANCOVA model included treatment, screening hsCRP, and the corresponding baseline value.

For safety assessments, COVID-19-related AEs were based on investigator assessment of AEs associated with COVID-19 and not limited to COVID-19 preferred terms.



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**Supplemental Table 1. Screening failure due to study eligibility criteria**

| Eligibility criteria reasons | N=562* |
|---|---|
| Screen failure due to AS bDMARD-IR study-specific criteria | n=215 |
| AS not confirmed and/or mNY criteria | n=43 |
| Total spinal ankylosis† | n=32 |
| Not bDMARD-IR | n=140 |
| Screen failure due to nr-axSpA study-specific criteria | n=307 |
| Common criteria | n=132 |
| Withdrew consent | n=17 |
| Insufficient disease activity | n=27 |
| Biologic washout | n=5 |
| Stable csDMARDs dose | n=1 |
| Stable concomitant background medications for axSpA | n=1 |
| Intake of prohibited medication | n=1 |
| Contraception related | n=2 |
| Exclusionary laboratory values | n=12 |
| Patient in good health as determined by PI | n=10 |
| Active or chronic infections | n=24 |
| History of exclusionary diseases | n=15 |
| Not suitable for participation per PI assessment | n=17 |

*Patients could have multiple criteria or multiple reasons for screening failure.
†Total spinal ankylosis was defined as bridging syndesmophytes (fusion) in a total sum of ≥5 segments of the C2-T1 or T12-S1 spine (eg, a case with 2 segments fused in the cervical and 3 segments fused in the lumbar spine would be considered positive for total spinal ankylosis).
AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; bDMARD, biologic disease-modifying antirheumatic drug; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; IR, inadequate response; mNY, modified New York; nr-axSpA, non-radiographic axial spondyloarthritis; PI, principal investigator.

**Supplemental Table 2. Primary and multiplicity-controlled secondary endpoints at week 14**

| | | Endpoints | Placebo (n=209) | Upadacitinib 15 mg once daily (n=211) | Difference vs placebo (95% CI) | P-value* |
|---|---|---|---|---|---|---|
| Primary | | ASAS40 | 18.2% | 44.5% | 26.4% (17.9%, 34.9%) | <0.0001 |
| Secondary | 1 | ASDAS (CRP) | −0.49 | −1.52 | −1.02 (−1.20, −0.85) | <0.0001 |
| | 2 | SPARCC MRI Spine† | −0.04 | −3.95 | −3.90 (−5.47, −2.33) | <0.0001 |
| | 3 | BASDAI50 | 16.7% | 43.1% | 26.4% (18.0%, 34.8%) | <0.0001 |
| | 4 | ASAS20 | 38.3% | 65.4% | 27.1% (17.9%, 36.3%) | <0.0001 |
| | 5 | ASDAS Inactive Disease | 1.9% | 12.8% | 10.9% (6.0%, 15.8%) | <0.0001 |
| | 6 | Total Back Pain | −1.47 | −3.00 | −1.53 (−1.96, −1.11) | <0.0001 |
| | 7 | Nocturnal Back Pain‡ | −1.52 | −3.21 | −1.69 (−2.14, −1.24) | <0.0001 |
| | 8 | ASDAS Low Disease Activity | 10.1% | 44.1% | 34.0% (26.2%, 41.8%) | <0.0001 |
| | 9 | BASFI | −1.09 | −2.26 | −1.17 (−1.55, −0.80) | <0.0001 |
| | 10 | ASAS Partial Remission | 4.3% | 17.5% | 13.2% (7.4%, 19.0%) | <0.0001 |
| | 11 | ASQoL§ | −2.03 | −5.10 | −3.07 (−3.90, −2.24) | <0.0001 |
| | 12 | ASAS Health Index‡ | −1.07 | −2.93 | −1.85 (−2.47, −1.24) | <0.0001 |
| | 13 | BASMI¶ | −0.16 | −0.48 | −0.32 (−0.46, −0.18) | <0.0001 |
| | 14 | MASES# | −1.1 | −2.6 | −1.5 (−2.0, −0.9) | <0.0001 |

Data are % or mean change from baseline unless noted otherwise. ASDAS low disease activity was defined as ASDAS (CRP) <2.1 and ASDAS inactive disease as ASDAS (CRP) <1.3.
*All p-values were statistically significant at the pre-specified two-sided 0.05 level with multiplicity adjustment.
†Assessed in n=186 in the placebo group; n=181 in the upadacitinib group with available baseline MRI data up to 3 days after the first dose of study drug and available week 14 MRI data up to the first dose of study drug in the open-label period.
‡Assessed in n=208 in the placebo group.
§Assessed in n=208 in the placebo group; n=210 in the upadacitinib group.
¶Assessed n=201 in the placebo group; n=205 in the upadacitinib group.
#Assessed in n=162 in the placebo group; and n=148 in the upadacitinib group with MASES >0 at baseline.
ASAS, Assessment of SpondyloArthritis international Society; ASAS20, Assessment of SpondyloArthritis international Society 20 response; ASAS40, Assessment of SpondyloArthritis international Society 40 response; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASQoL, Ankylosing Spondylitis Quality of Life Score; BASDAI50, at least 50% improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CI, confidence interval; CRP, C-reactive protein; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; SPARCC, Spondyloarthritis Research Consortium of Canada.

**Supplemental Table 3. Additional endpoints at week 14**

| Endpoints | Placebo (n=209) | Upadacitinib 15 mg once daily (n=211) | Difference vs placebo (95% CI) | P-value‡ |
|---|---|---|---|---|
| Patient Global Assessment of Disease Activity* | −1.38 | −2.97 | −1.59 (−2.01, −1.17) | <0.0001 |
| Fatigue/tiredness (BASDAI Question 1)* | −1.44 | −2.56 | −1.13 (−1.55, −0.70) | <0.0001 |
| Patient Assessment of Back Pain (BASDAI Question 2)* | −1.53 | −3.02 | −1.48 (−1.91, −1.06) | <0.0001 |
| Peripheral pain/swelling (BASDAI Question 3)* | −1.17 | −2.32 | −1.15 (−1.59, −0.72) | <0.0001 |
| Tenderness (BASDAI Question 4)* | −1.45 | −2.76 | −1.31 (−1.76, −0.86) | <0.0001 |
| Severity of morning stiffness (BASDAI Question 5)* | −1.67 | −3.08 | −1.41 (−1.86, −0.96) | <0.0001 |
| Duration of morning stiffness (BASDAI Question 6)* | −1.54 | −2.80 | −1.26 (−1.72, −0.80) | <0.0001 |
| Tender joint count† | −1.2 | −2.3 | −1.1 (−1.8, −0.4) | 0.0022 |
| Swollen joint count† | −0.4 | −0.9 | −0.6 (−0.9, −0.2) | 0.0026 |

Data are % or mean change from baseline unless noted otherwise.
*MMRM analysis was used.
†Assessed in n=201 in the placebo group; n=205 in the upadacitinib group. ANCOVA analysis was used.
‡Nominal p-values are presented (without adjustment for multiplicity).
ANCOVA, Analysis of covariance; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CI, confidence interval; MMRM, mixed-effect model for repeated measures.



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**Supplemental Table 4. Treatment-emergent COVID-19-related AEs through week 14**

| | Placebo (n=209) | Upadacitinib 15 mg once daily (n=211) |
|---|---|---|
| Any AE | 6 (2.9%) | 12 (5.7%) |
| Gastrointestinal disorders | 0 | 1 (0.5%) |
| Diarrhea | 0 | 1 (0.5%) |
| Infections and infestations | 6 (2.9%) | 12 (5.7%) |
| Asymptomatic COVID-19 | 1 (0.5%) | 3 (1.4%) |
| COVID-19 | 4 (1.9%) | 7 (3.3%) |
| COVID-19 pneumonia | 0 | 4 (1.9%) |
| Urinary tract infection | 1 (0.5%)* | 0 |

Data are n (%). Treatment-emergent COVID-19-related AEs are presented by primary MedDRA 24.0 system organ class and preferred term. Patients were counted once for each row, regardless of the number of events they had.
*An AE with the preferred term "urinary tract infection" was incorrectly attributed to COVID-19 by the site. Therefore, 5 subjects in the placebo group had COVID-19-related AEs.
AE, adverse event; COVID-19, coronavirus disease of 2019; MedDRA, Medical Dictionary for Regulatory Activities.



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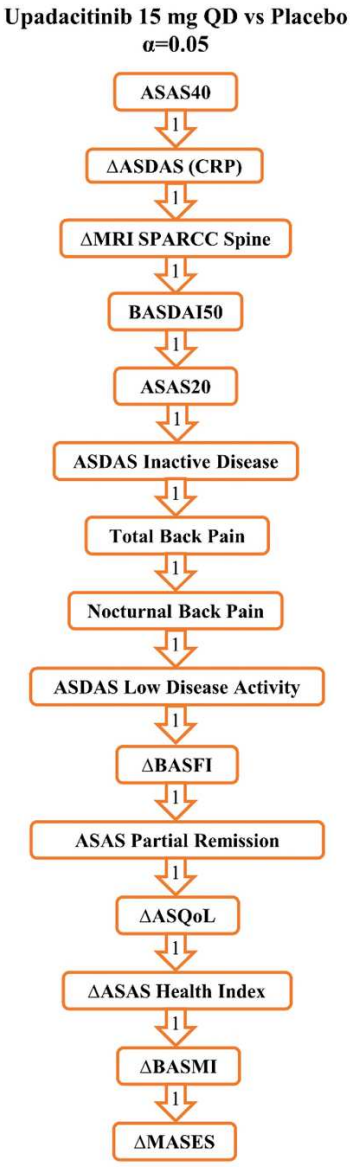
**Supplemental Table 5. Overview of treatment-emergent COVID-19-related AEs through week 14**

| Patient | Age/ Sex | Country | Study Treatment | Vaccination Status | Severity* | Causality† | Documented Treatment(s) For COVID-19 AEs‡ | Hospitalization | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 43M | Russia | UPA | No | Severe | NRP | Oral amoxicillin/clavulanic acid; IV dexamethasone; oral acetylcysteine, oral metronidazole, oral methylprednisolone; subcutaneous olokizumab; oral alimemazine tartrate; oral riamilovir; oral ascorbic acid; oral colecaliciferol; subcutaneous bemiparin sodium | Yes | Resolved |
| **2** | 38M | Czechia | UPA | No | Severe | NRP | Oral acetylcysteine; IV ambroxol hydrochloride; oral and IV amoxicillin/clavulanic acid; inhaled ipratropium bromide; oral codeine phosphate; oral erdosteine; oral and IV clarithromycin; IV aminophylline; inhaled salbutamol; oral cefuroxime axetil | Yes | Resolved |
| **3** | 29M | Ukraine | UPA | No | Moderate | NRP | Oral acetylcysteine, IV ambroxol, oral amoxicillin/clavulanate; oral arginine citrate/betaine/betaine hydrochloride; IV dexamethasone; oral saccharomyces boulardii; IV levofloxacine; IV meropenem | Yes | Resolved |
| **4** | 70F | Hungary | UPA | No | Moderate | NRP | Oral acetylcysteine; oral dexamethasone; oral paracetamol/tramadol; oral favipiravir; IV clarithromycin; oral methylprednisolone; IV remdesivir; IV ceftriaxone | Yes | Resolved |
| **5** | 45M | Russia | PBO | No | Mild | NRP | Oral ascorbic acid; oral ergocalciferol | No | Resolved |
| **6** | 50F | Spain | PBO | No | Severe | NRP | Oral domperidone; oral paracetamol | No | Resolved |
| **7** | 34M | Ukraine | UPA | No | Severe | NRP | Oral paracetamol | No | Resolved |
| **8** | 61F | Bulgaria | UPA | No | Mild | RP | Oral ascorbic acid | No | Resolved |
| **9** | 49F | Bulgaria | UPA | No | Severe | NRP | Oral dipyridamole; oral acetylsalicylic acid; oral clarithromycin | No | Resolved |
| **10** | 34M | USA | UPA | No | Mild | NRP | Oral azithromycin; oral methylprednisolone | No | Resolved |
| **11** | 47M | Czechia | PBO | No | Moderate | NRP | No specific treatment given | No | Resolved |
| **12** | 39M | Argentina | PBO | No | Mild | NRP | No specific treatment given | No | Resolved |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **13** | 65M | Argentina | PBO | No | Moderate | NRP | No specific treatment given | No | Resolved |
| **14**§ | 60F | Mexico | PBO | No | N/A | N/A | No specific treatment given | No | Resolved |
| **15** | 47M | Czechia | UPA | No | Moderate | NRP | No specific treatment given | No | Resolved |
| **16** | 42M | Argentina | UPA | Yes | Mild | NRP | No specific treatment given | No | Resolved |
| **17** | 38M | Germany | UPA | No | Mild | NRP | No specific treatment given | No | Resolved |
| **18** | 26M | Ukraine | UPA | No | Mild | NRP | No specific treatment given | No | Resolved |

Other than for COVID-19-related AEs, no clinically meaningful differences were observed in terms of safety events for Eastern European vs non-Eastern European patients.
*Severity based on CTCAE v4.03. Risk factors for patients with severe COVID-19 included advanced age, hypertension, and obesity.
†Relationship to study drug based on investigator assessment.
‡Treatment as reported by the investigator.
§Not real COVID case; an AE with the preferred term “urinary tract infection” was incorrectly attributed to COVID-19 by the site.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; IV, intravenous; N/A, not applicable; NRP, no reasonable possibility; PBO, placebo; RP, reasonable possibility; UPA, upadacitinib.

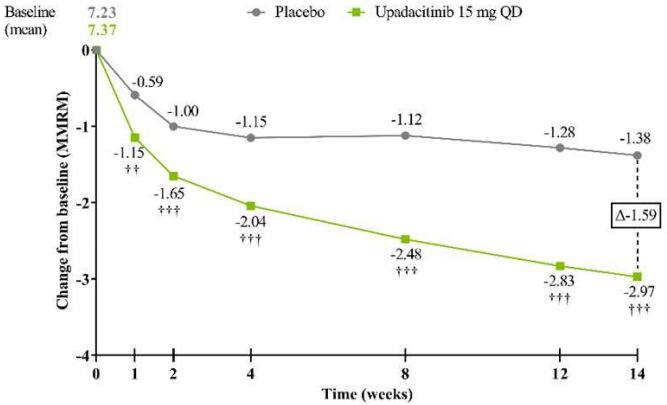



## Supplemental Figure 1. Multiplicity-controlled sequential testing procedure of primary and secondary endpoints

The multiplicity-controlled primary and secondary endpoints were tested in a sequential manner with an assigned α=0.05. Significance was claimed for a lower ranked endpoint only if the previous endpoint in the sequence met statistical significance. ASDAS low disease activity was defined as ASDAS (CRP) <2.1 and ASDAS inactive disease as ASDAS (CRP) <1.3.
ASAS, Assessment of SpondyloArthritis international Society; ASAS20, Assessment of SpondyloArthritis international Society 20 response; ASAS40, Assessment of SpondyloArthritis international Society 40 response; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASQoL, Ankylosing Spondylitis Quality of Life Score; BASDAI50, at least 50% improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C-reactive protein; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; SPARCC, Spondyloarthritis Research Consortium of Canada.

**ASAS Components**

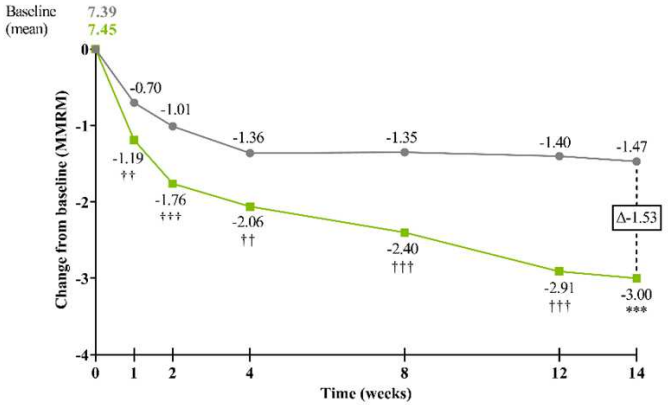
**A** **Patient's Global Assessment of Disease Activity (NRS 0–10)**




**Number of patients**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 204 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 208 | 207 | 208 | 207 | 207 | 206 |

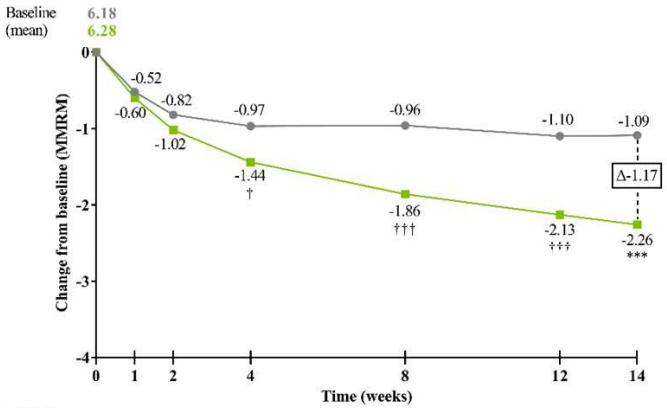
**B** **Patient's Assessment of Total Back Pain (NRS 0-10)**




**Number of patients**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 204 | 203 | 208 | 201 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 208 | 207 | 208 | 207 | 207 | 206 |

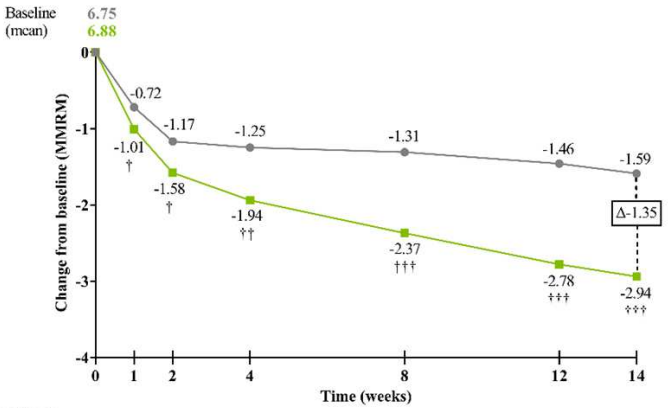
**C** **BASFI**




**Number of patients**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 204 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 208 | 207 | 208 | 207 | 207 | 206 |

**D** **Morning Stiffness (NRS 0-10)**




**Number of patients**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 205 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 209 | 207 | 208 | 207 | 207 | 206 |

**Supplemental Figure 2. Change from baseline in individual ASAS components (A–D) through week 14**

Patient's global assessment of disease activity (A) is both an ASAS and ASDAS component. Patient's assessment of total back pain (B) and BASFI (C) were multiplicity-controlled endpoints at week 14. (B) Total back pain was defined on a NRS (0–10) based on the question, "What is the amount of back pain that you experienced at any time during the last week?" (D) Inflammation related to morning stiffness was defined as the mean of questions 5 and 6 of the BASDAI. MMRM analysis was used, and the numbers of patients were as observed at each visit.
Significant in multiplicity-controlled analysis: ***p<0.0001. Without adjustment for multiplicity (nominal): †p<0.05, ††p<0.001, †††p<0.0001.
ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; MMRM, mixed-effect model for repeated measures; NRS, numeric rating scale; QD, once daily.



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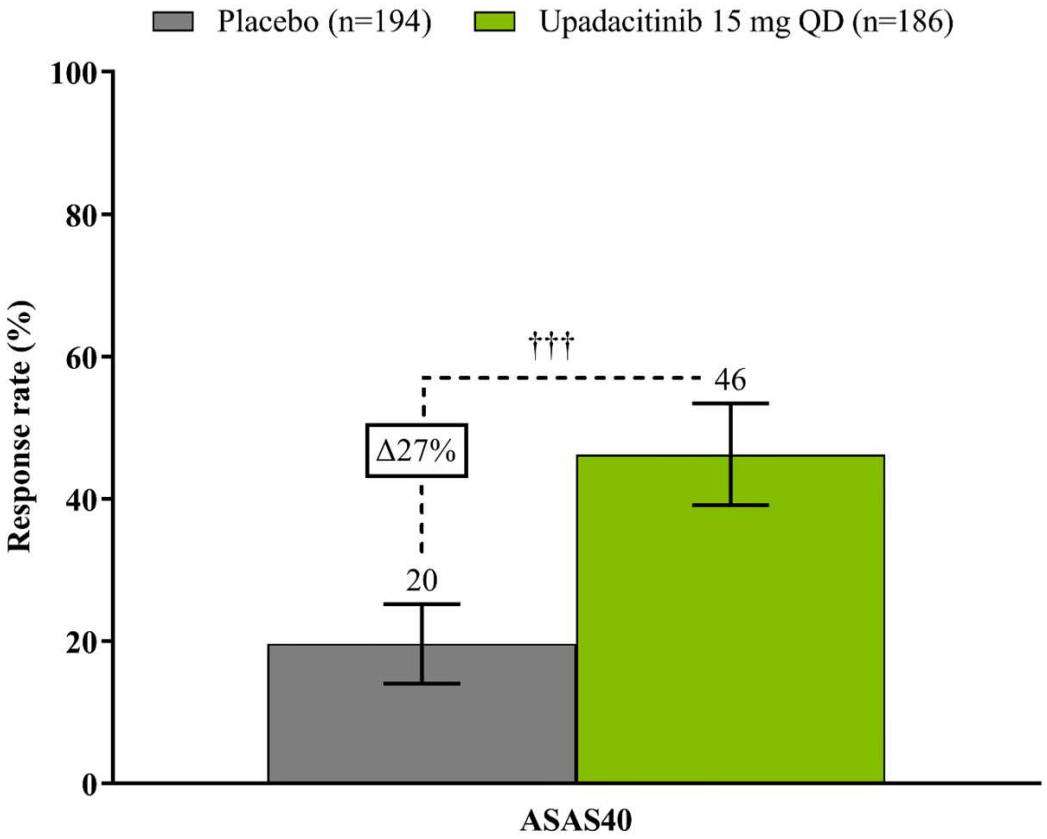


**Supplemental Figure 3. ASAS40 response at week 14 in the per-protocol analysis set**

The per-protocol analysis set included patients without major protocol deviations. NRI-MI analysis was used. Error bars show 95% CI. Without adjustment for multiplicity (nominal): †††p<0.0001.
ASAS40, Assessment of SpondyloArthritis international Society 40 response; CI, confidence interval; NRI-MI, non-responder imputation incorporating multiple imputation; QD, once daily.



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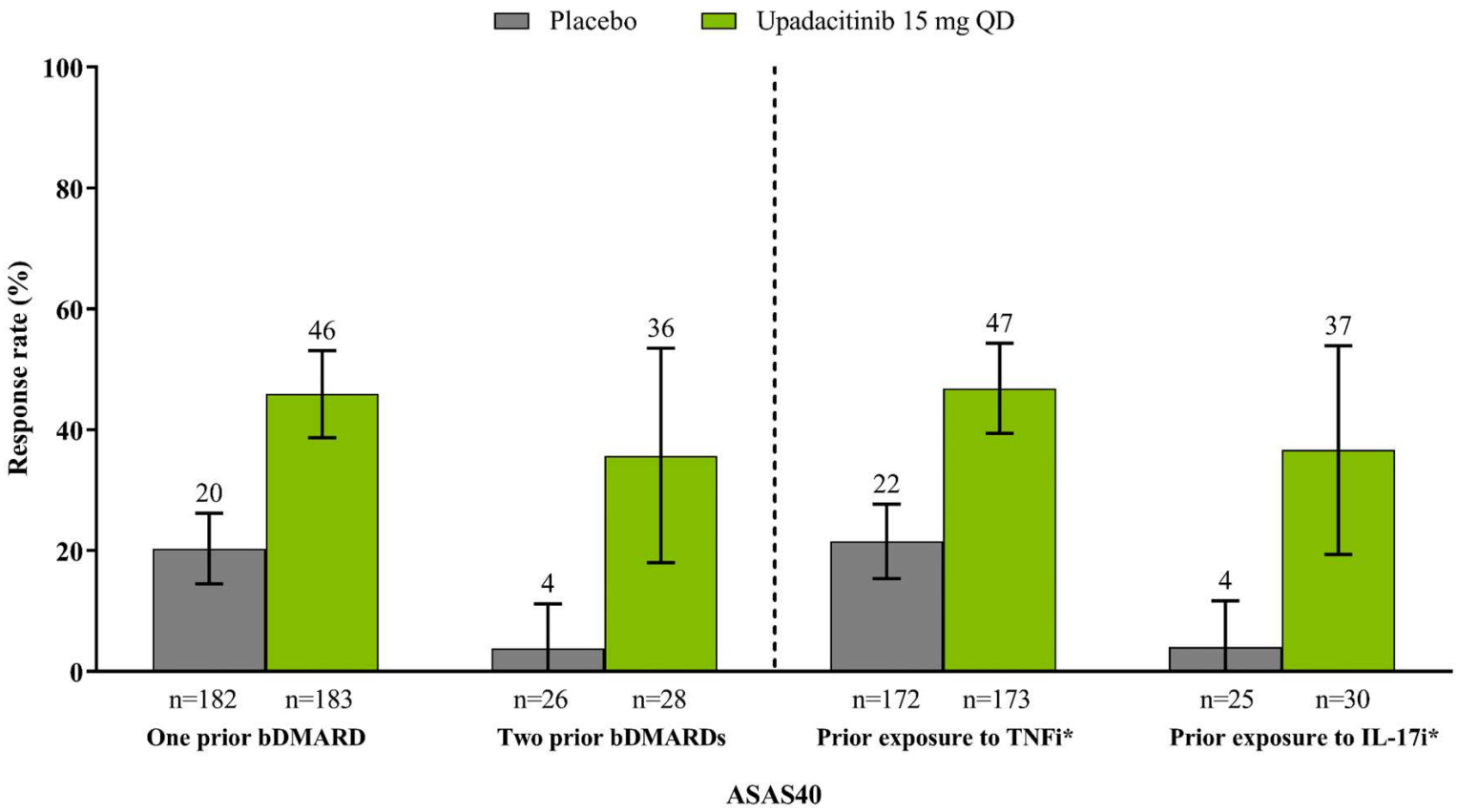
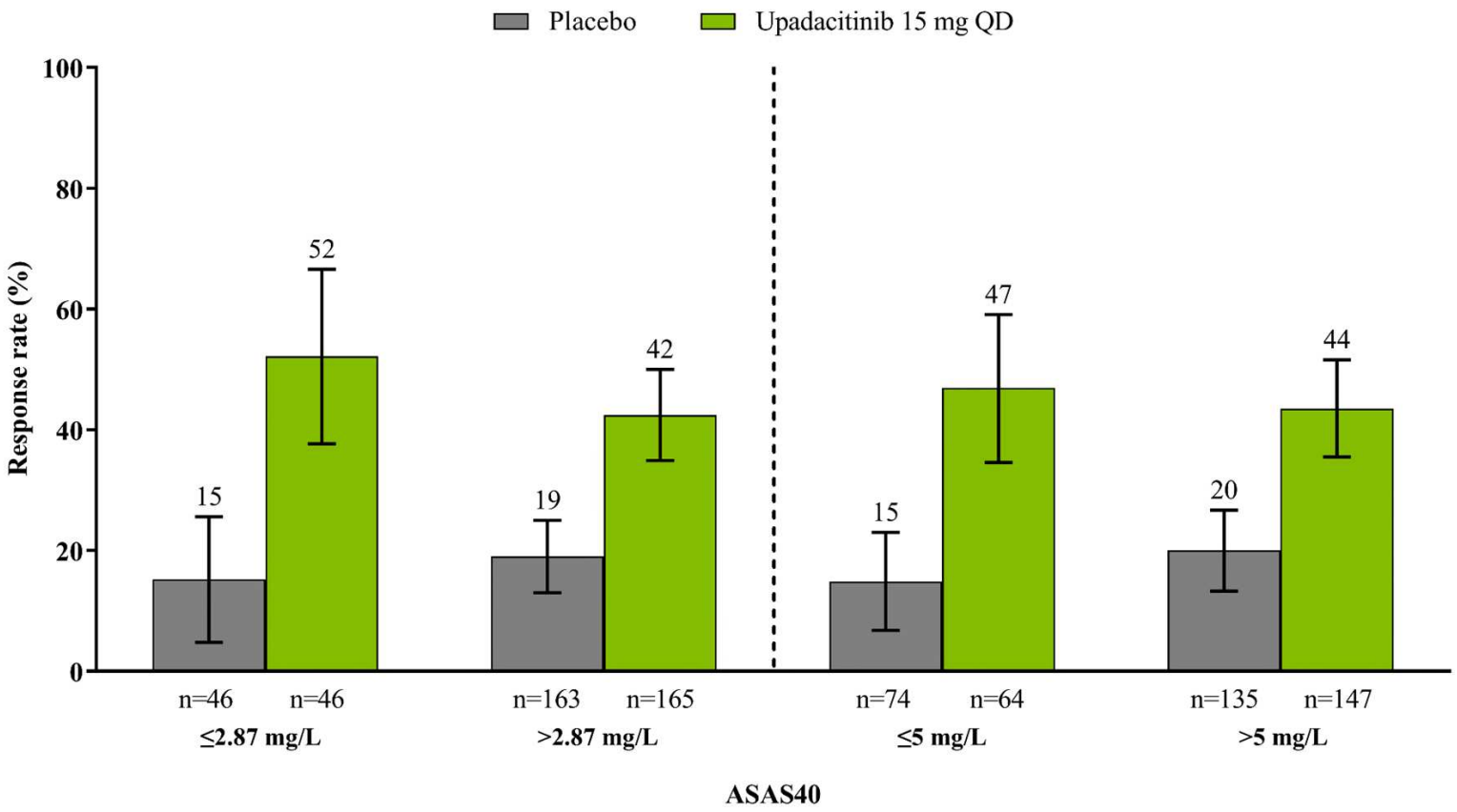



**Supplemental Figure 4. Subgroup analysis of ASAS40 response at week 14 by number and type of prior bDMARDs use**

NRI-MI analysis was used. Error bars show 95% CI.
*Prior exposure was based on exposure to one or two TNFi or one or two IL-17i.
ASAS40, Assessment of SpondyloArthritis international Society 40 response; bDMARD, biologic disease-modifying antirheumatic drug; CI, confidence interval; IL-17, interleukin-17 inhibitor; NRI-MI, non-responder imputation incorporating multiple-imputation; QD, once daily; TNFi, tumor necrosis factor inhibitor.




**Supplemental Figure 5. Subgroup analysis of ASAS40 response at week 14 by hsCRP level at screening**

NRI-MI analysis was used. Error bars show 95% CI.
ASAS40, Assessment of SpondyloArthritis international Society 40 response; CI, confidence interval; hsCRP, high-sensitivity C-reactive protein; NRI-MI, non-responder imputation incorporating multiple-imputation; QD, once daily.



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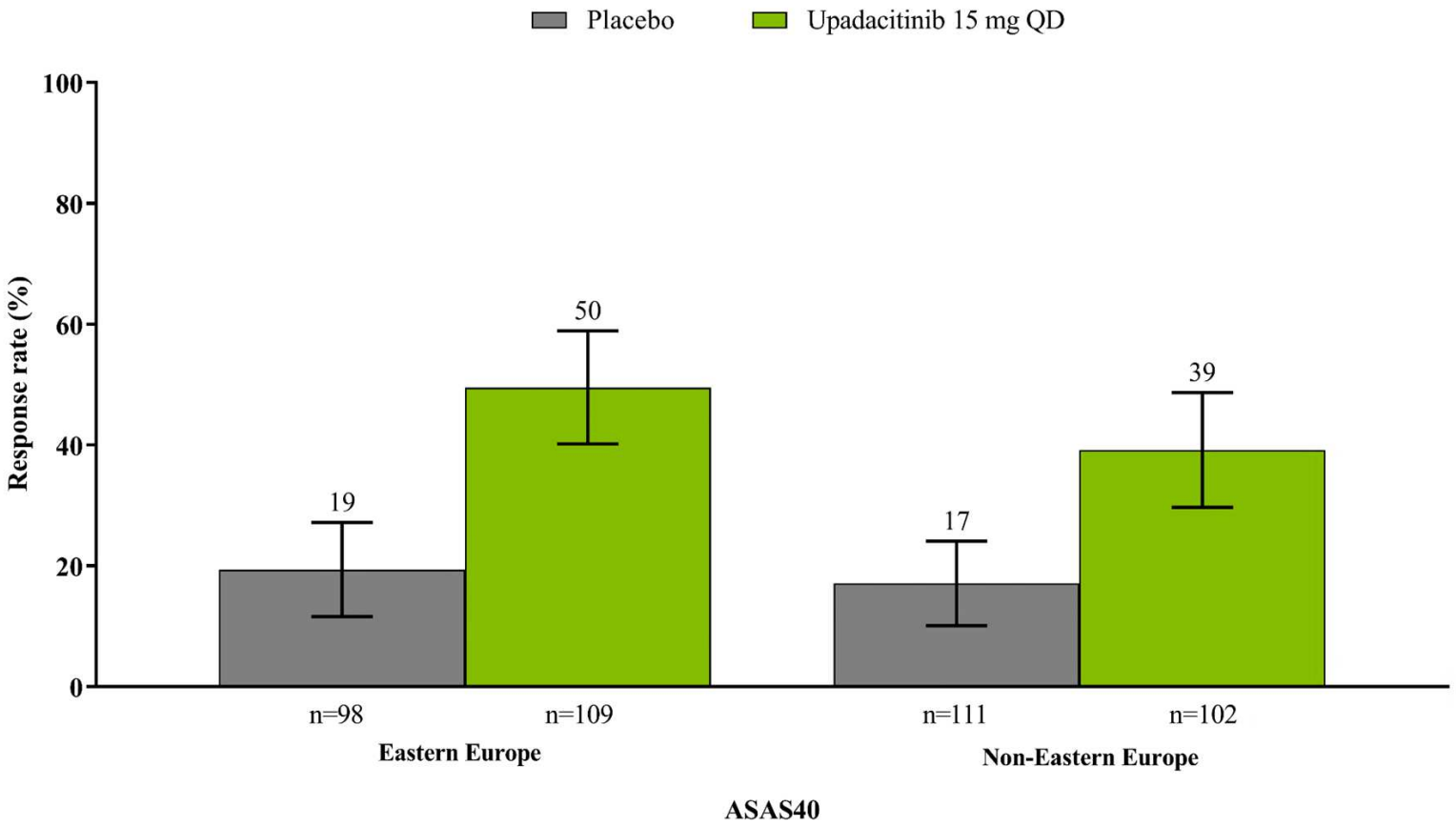
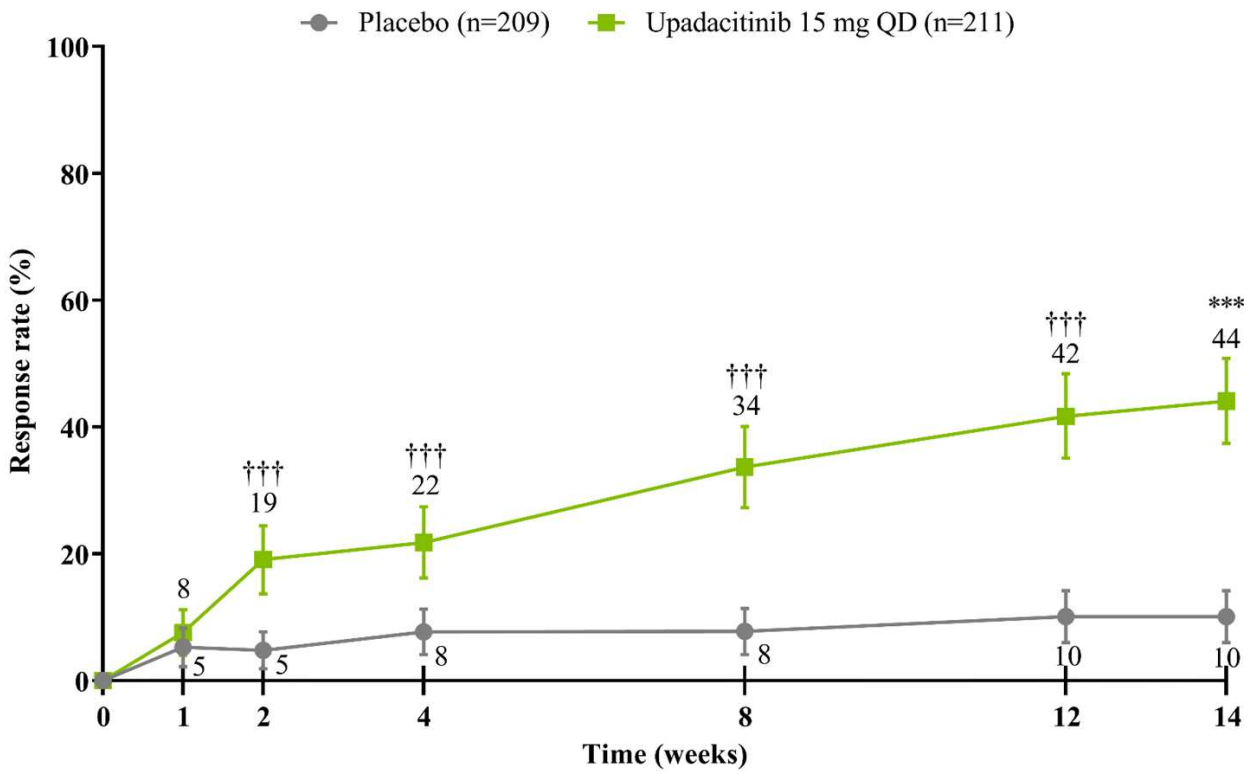


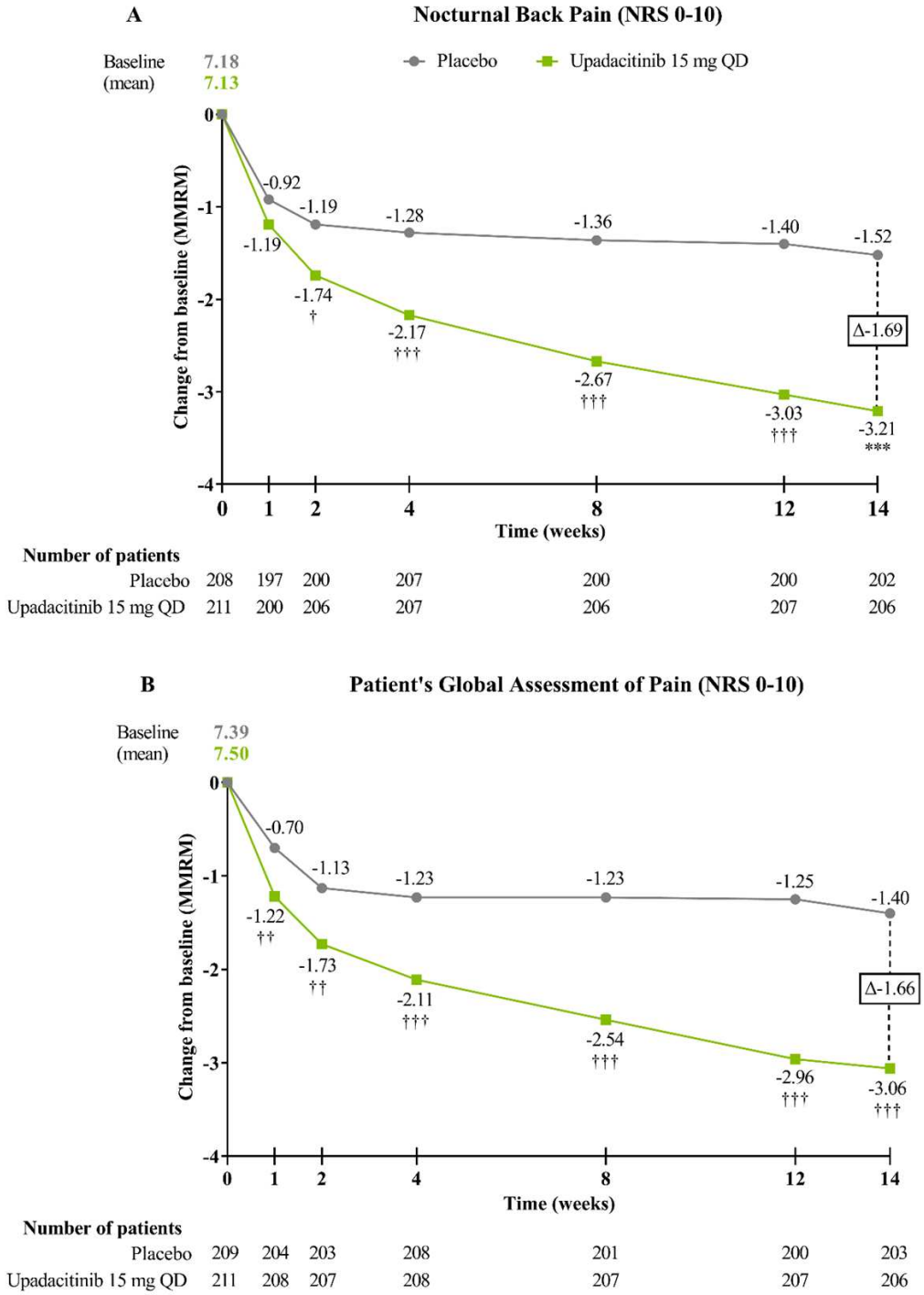

**Supplemental Figure 6. Subgroup analysis of ASAS40 response at week 14 between Eastern European vs Non-Eastern European patients**

NRI-MI analysis was used. Error bars show 95% CI.
ASAS40, Assessment of SpondyloArthritis international Society 40 response; CI, confidence interval; NRI-MI, non-responder imputation incorporating multiple-imputation; QD, once daily.



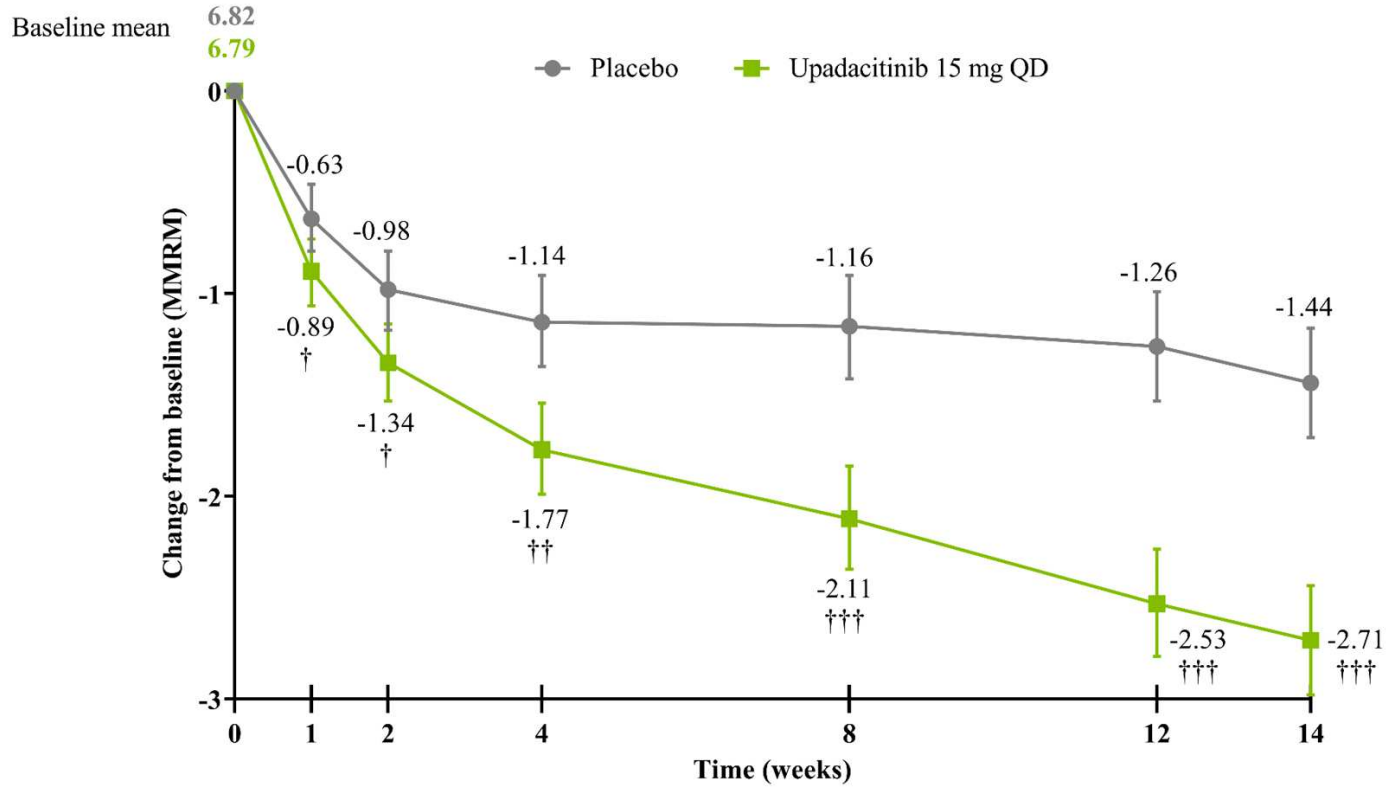

**Supplemental Figure 7. ASDAS low disease activity (<2.1) through week 14**

NRI-MI analysis was used. Error bars show 95% CI. ASDAS low disease activity was defined as ASDAS (CRP) <2.1.
Significant in multiplicity-controlled analysis: ***p<0.0001. Without adjustment for multiplicity (nominal): †††p<0.0001.
ASDAS, Ankylosing Spondylitis Disease Activity Score; CI, confidence interval; CRP, C-reactive protein; NRI-MI, non-responder imputation incorporating multiple-imputation; QD, once daily.




## Supplemental Figure 8. Pain responses through week 14

(A) Mean change from baseline in nocturnal back pain and (B) Patient's global assessment of pain through week 14. Total back pain and peripheral pain/swelling responses are shown in Supplemental Figures 2B and 10C. (A, B) MMRM analysis was used, and the numbers of patients were as observed at each visit.
Significant in multiplicity-controlled analysis: ***p<0.001. Without adjustment for multiplicity (nominal): †p<0.05, ††p<0.001, †††p<0.0001.
MMRM, mixed-effect model for repeated measures; NRS, numeric rating scale; QD, once daily.



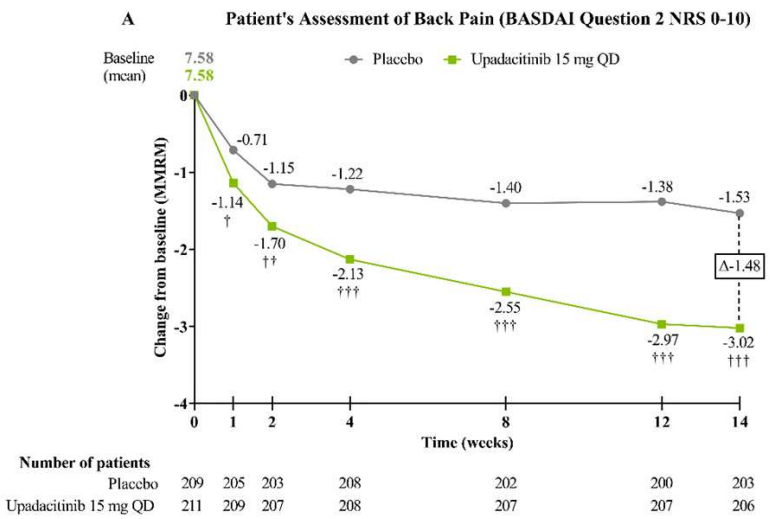

**Number of patients**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 205 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 209 | 207 | 208 | 207 | 207 | 206 |

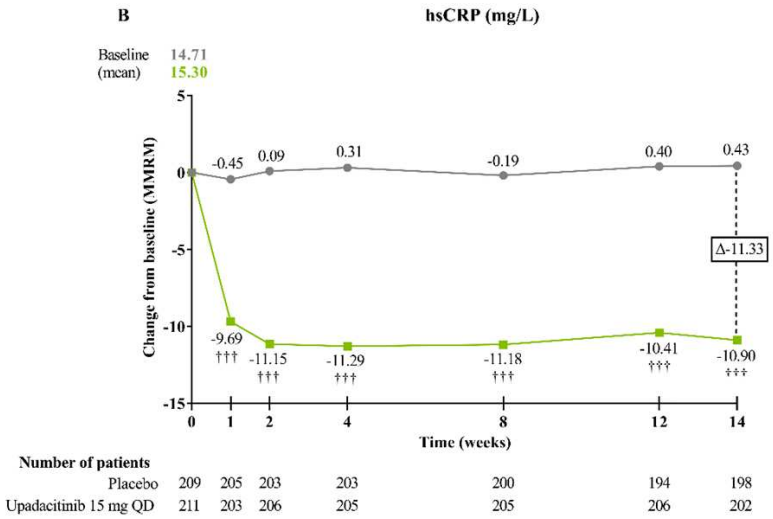
**Supplemental Figure 9. BASDAI through week 14**

MMRM analysis was used, and the numbers of patients were as observed at each visit. Error bars show 95% CI. Without adjustment for multiplicity (nominal): †p<0.05, ††p<0.001, †††p<0.0001.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CI, confidence interval; MMRM, mixed-effect model for repeated measures; QD, once daily.

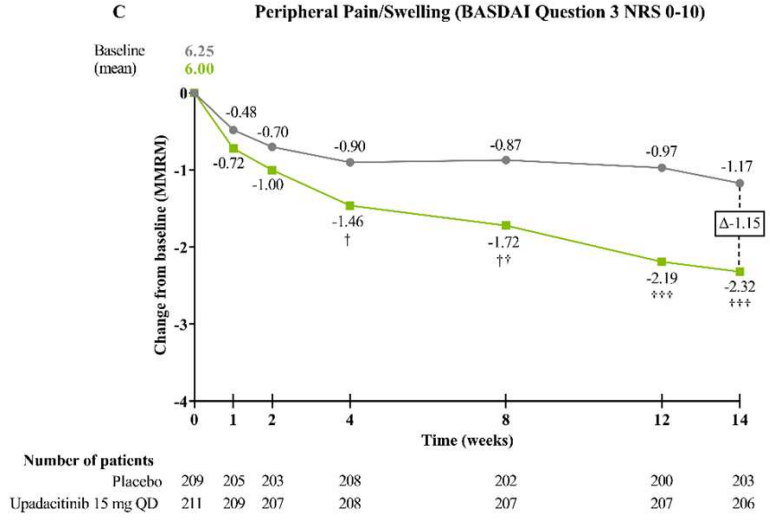
**ASDAS Components**



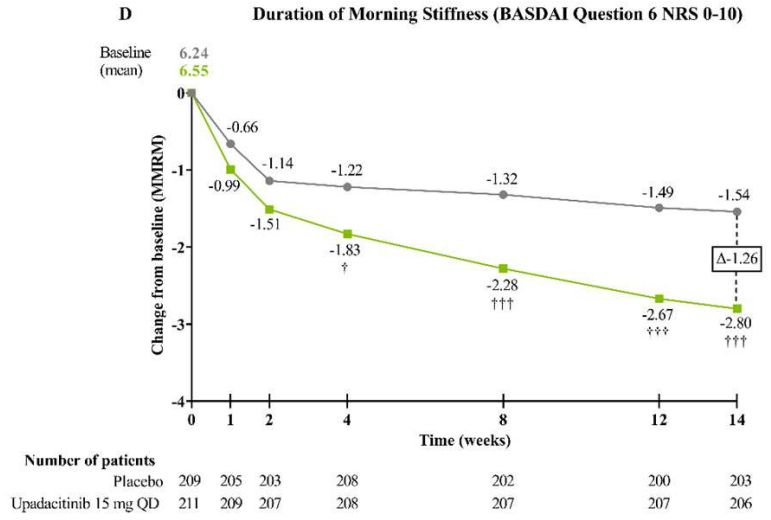

| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 205 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 209 | 207 | 208 | 207 | 207 | 206 |




| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 205 | 203 | 203 | 200 | 194 | 198 |
| Upadacitinib 15 mg QD | 211 | 203 | 206 | 205 | 205 | 206 | 202 |




| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 205 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 209 | 207 | 208 | 207 | 207 | 206 |




| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 205 | 203 | 208 | 202 | 200 | 203 |
| Upadacitinib 15 mg QD | 211 | 209 | 207 | 208 | 207 | 207 | 206 |

**Supplemental Figure 10. Change from baseline in individual ASDAS components (A–D) through week 14**

Patient's global assessment of disease activity is both an ASAS and ASDAS component and is shown in Supplementary Figure 2A. MMRM analysis was used, and the numbers of patients were as observed at each visit.
Without adjustment for multiplicity (nominal): †p<0.05, ††p<0.001, †††p<0.0001.
ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high-sensitivity C-reactive protein; MMRM, mixed-effect model for repeated measures; NRS, numeric rating scale; QD, once daily.



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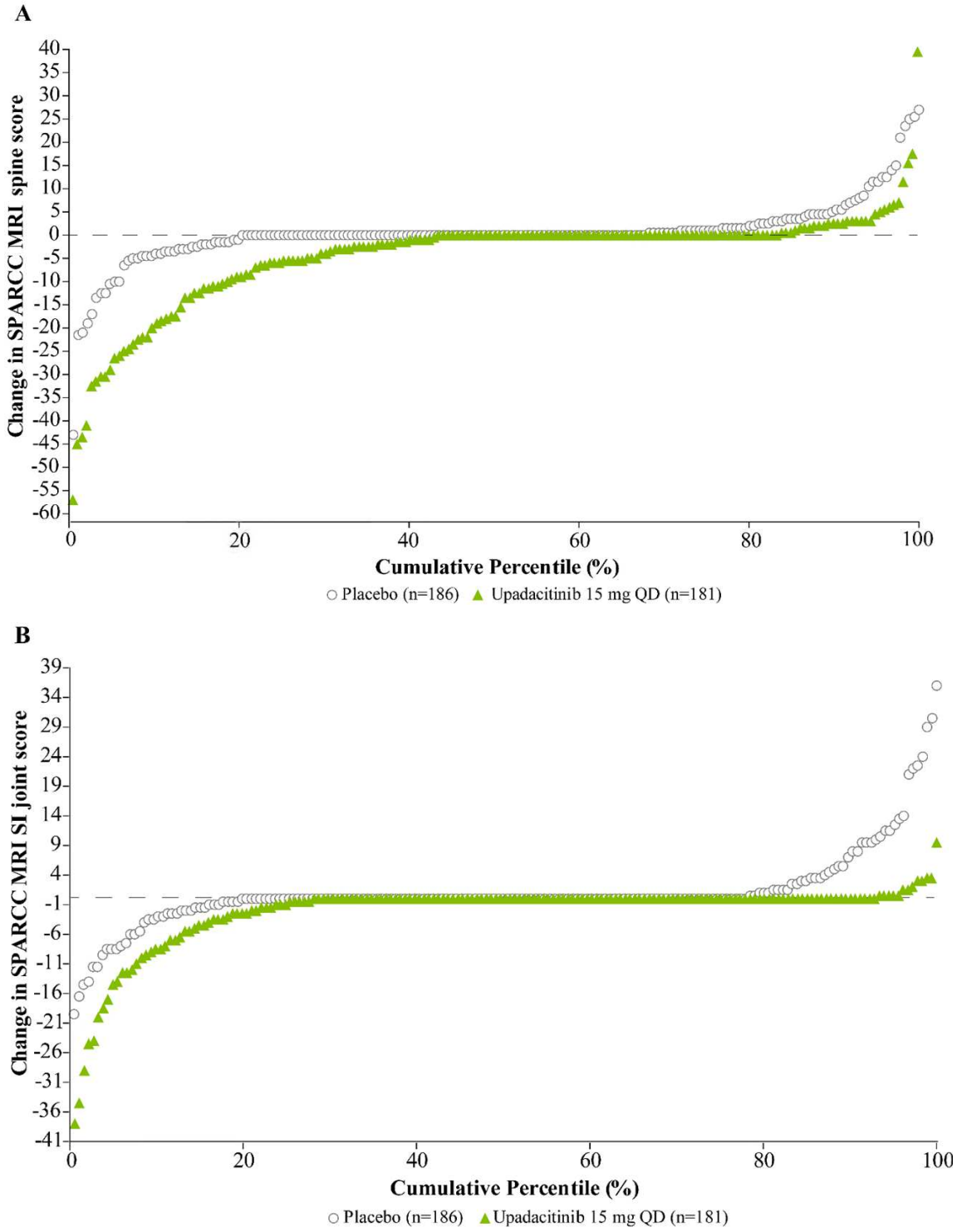


**Supplemental Figure 11. Cumulative probability plots for SPARCC MRI spine and SI joint scores**

(A) Cumulative probability of change in SPARCC MRI spine and (B) SI joint scores. MRIs were independently assessed by two readers blinded to treatment allocation and imaging time points. Discrepancies between the readers were resolved through adjudication by a third reader if scoring differences exceeded a certain mean

absolute difference threshold. The adjudication trigger for MRI of the spine was >14 and for MRI of the sacroiliac joints was >8.
MRI, magnetic resonance imaging; QD, once daily; SI, sacroiliac; SPARCC, Spondyloarthritis Research Consortium of Canada.



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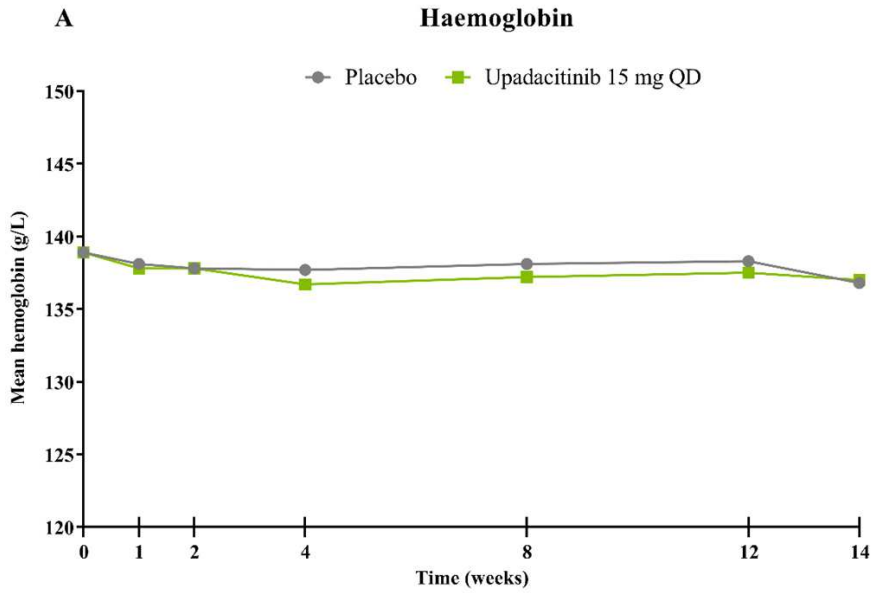
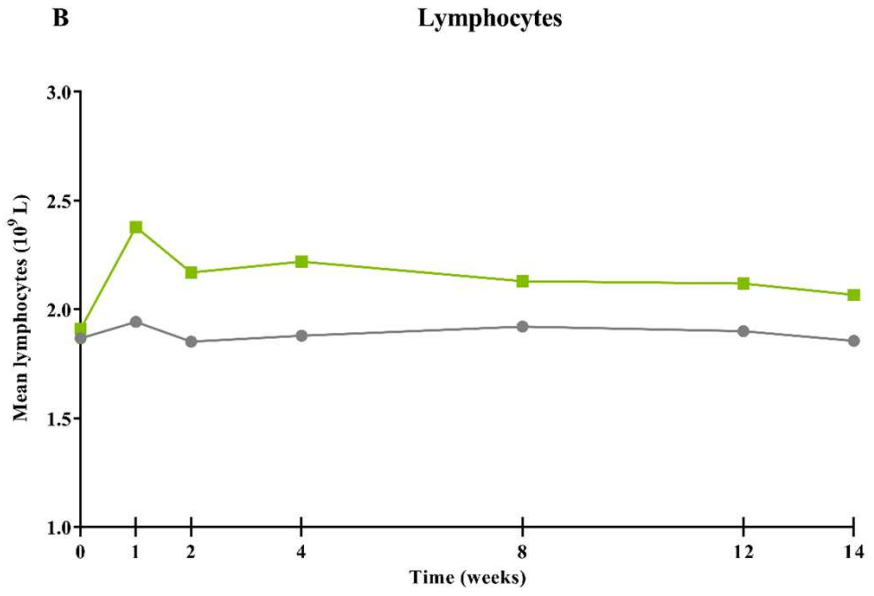



| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 200 | 201 | 207 | 200 | 194 | 197 |
| Upadacitinib 15 mg QD | 211 | 202 | 204 | 207 | 202 | 200 | 197 |

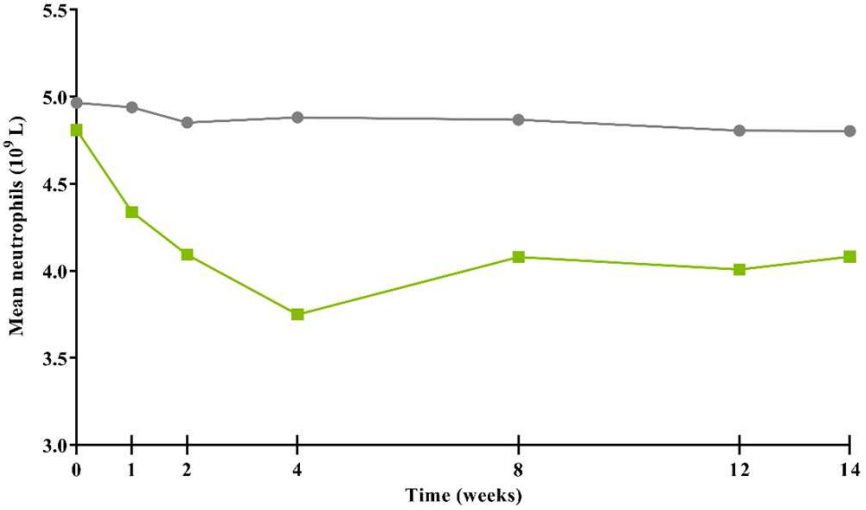



| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 200 | 201 | 207 | 200 | 194 | 197 |
| Upadacitinib 15 mg QD | 211 | 202 | 204 | 207 | 201 | 199 | 197 |



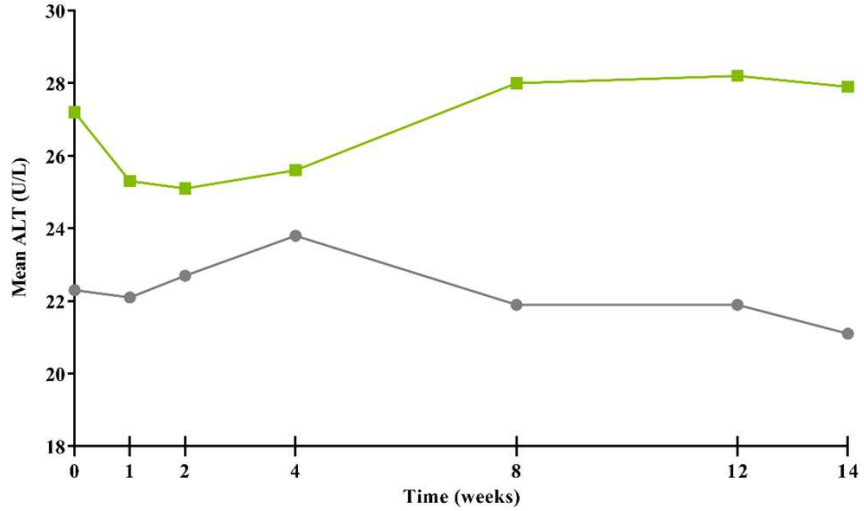
van der Heijde D, *et al. Ann Rheum Dis* 2022; 81:1515–1523. doi: 10.1136/ard-2022-222608

**C** **Neutrophils**

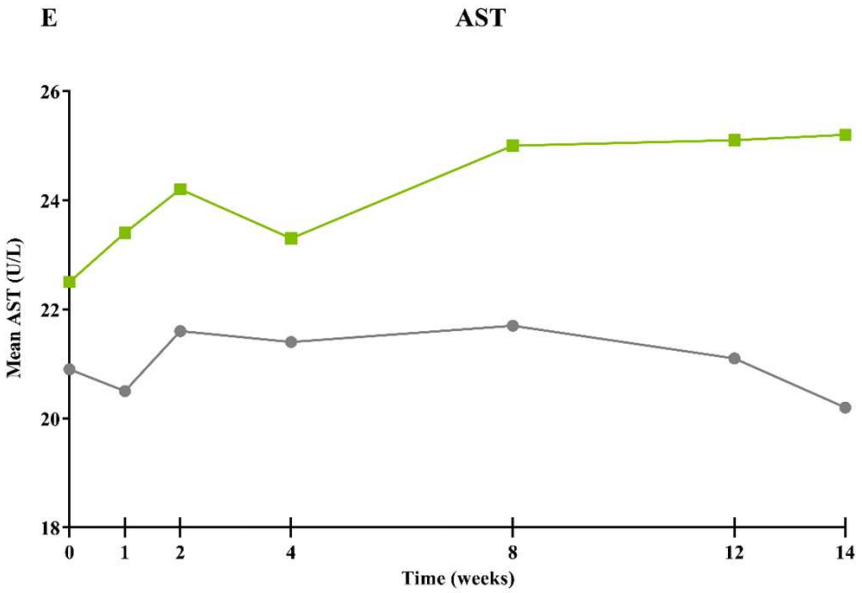



| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 200 | 201 | 207 | 200 | 194 | 197 |
| Upadacitinib 15 mg QD | 211 | 202 | 204 | 207 | 201 | 200 | 197 |

**D** **ALT**




| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 206 | 202 | 208 | 201 | 198 | 202 |
| Upadacitinib 15 mg QD | 211 | 204 | 205 | 207 | 206 | 206 | 205 |




| Number of patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Placebo | 209 | 203 | 203 | 208 | 200 | 198 | 202 |
| Upadacitinib 15 mg QD | 211 | 203 | 206 | 207 | 205 | 204 | 206 |

**Supplemental Figure 12. Mean laboratory levels through week 14**

(A) Mean haemoglobin, (B) lymphocyte, (C) neutrophil, (D) ALT, and (E) AST levels through week 14. ALT, alanine aminotransferase; AST, aspartate aminotransferase; QD, once daily.